Review Article

Is the Wada test necessary prior to epilepsy surgery?

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ABSTRACT

The Wada test was initially used to identify the hemisphere of language dominance prior to epilepsy surgery, but was subsequently applied to identify patients at risk of amnesia after temporal resection. The Wada test was later found useful in lateralizing the epileptogenic zone, predicting postoperative memory function, and predicting postoperative seizure control. The Wada test became more widely used, and in many centers became a standard component of the presurgical evaluation of epilepsy. Yet, several problems and disadvantages have surrounded the Wada test, including absence of standardized technique, overestimation of postoperative deficits, and risks and discomforts related to the invasive nature of the procedure. The Wada test may be omitted in patients who have excellent localization of the epileptogenic zone and who do not appear at risk for postoperative memory or language compromise. In addition, there is a promising alternative in functional magnetic resonance imaging (fMRI), which has already demonstrated excellent agreement with the Wada test for language dominance. Progress is being made in memory fMRI as well. The Wada test identifies the capacity of one hemisphere to sustain memory, and language functions while the other hemisphere is inactivated, while fMRI identifies regions activated by language or memory tasks. Some of these activated regions may not be essential for the activating tasks. Before fMRI can fully replace the Wada test it has to specifically identify those activated regions that are essential for memory or language function, and also measure the memory reserves of the hemisphere contralateral to surgery.

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The intracarotid sodium amobarbital procedure or Wada test has been the standard method for preoperative language localization since the technique was first described by Juhn Wada.[1,2] The Wada test involves the injection of amobarbital in the internal carotid artery, thereby inactivating the part of the hemisphere supplied by the anterior and middle cerebral arteries, and occasionally the posterior cerebral artery as well. During the period of inactivation, the language functions of the contralateral hemisphere can be examined. The procedure is usually repeated in the other hemisphere after 30 minutes or the next day. Widespread application of the Wada test in epilepsy patients undergoing presurgical evaluation demonstrated that approximately 90% of right-handed individuals are left hemisphere dominant for language. If patients with early left hemisphere insults are excluded, the percentage increases to 96%. If only patients with right temporal foci are studied, close to 100% of right-handed individuals would have left hemisphere dominance for language. On the other hand, left-handed individuals are more likely to have atypical language representation, with either right hemisphere dominance or bilateral representation.[3] Because of the above numbers, many centers reserved the use of the Wada test in language lateralization for patients in whom atypical lateralization was deemed likelier.

The application of the Wada test for investigation of memory reserves in each hemisphere was a later addition.[4] Memory items are presented during hemispheric anesthesia, then the patient is asked to recall the items following recovery from the anesthetic effect. The use of the Wada test for memory testing also varies between centers.[5,6] Some centers perform the Wada test for memory in all patients considering epilepsy surgery. However, in other centers the Wada test is restricted to

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patients suspected of not having sufficient memory reserves in the hemisphere contralateral to surgery. The Wada test was found to have a predictive value with respect to memory outcome postoperatively.[7-9] The relationship between Wada memory performance and postoperative memory outcome was more likely to be seen when asymmetry measures rather than absolute scores were used.[7,9,10] The Wada memory performance was also found to have value for lateralization of the pathologic presumably epileptogenic hippocampus,[11-17] and for the prediction of postoperative seizure control.[18-20] However, the lateralizing power of the Wada test may depend on mesial temporal localization of the epileptogenic zone.[21,22] One study took advantage of the absence of Wada memory asymmetry in neocortical temporal lobe epilepsy to suggest that the Wada test could help distinguish lateral and mesial temporal lobe foci.[21]

The Wada test has a number of limitations, disadvantages and risks, resulting in the search for alternative procedures. The validity of the Wada test for inactivation of the hippocampus was questioned because the hippocampus is largely supplied from the posterior cerebral artery.[23,24] A selective posterior cerebral artery amobarbital procedure was devised to address this limitation.[25-27] However, single photon emission computed tomography (SPECT) and electroencephalogram (EEG) evidence suggested that the hippocampus was inactivated even when it was not directly anesthetized.[28-32] Despite that determination, the hippocampal inactivation does not seem to be consistent in all patients, which may affect Wada memory results.[33,34] The specificity of the Wada test in identifying patients at risk of amnesia from temporal lobectomy was also questioned, because of individuals who failed the Wada memory testing yet were not amnestic after surgery.[35,36] The Wada test may overestimate the postoperative memory deficit, possibly because of anesthetized cerebral structures that are not included in the surgical resection. In order to restrict the inactivation to regions targeted for resection, selective anterior cerebral Wada procedures were devised.[37-40] These procedures may possibly reduce unnecessary denial of surgery due to exaggeration of the risk of amnesia.[39] Another limitation of the Wada test is the absence of methodological standardization across centers.[6] Methodological differences include the type and dose of anesthetic used,[41,42] the interval between the testing of the 2 hemispheres,[43] the order of hemisphere injection, the type and number of stimuli used,[44] timing of memory testing,[45,46] and scoring system.[16] Many of these methodological variations may have an impact on results and result interpretation.[43-46] These differences makes it difficult to generalize findings across centers using different techniques. Finally, the Wada test has discomforts and risks, including risk of arterial injury and cerebral dissection.[47] Because of all the above, some centers restrict the Wada test to difficult patients, with poor baseline memory (documented on neuropsychological testing), likely atypical language representation (for example in left-handed), or unclear localization of the epileptogenic zone (bitemporal independent foci, bitemporal structural or functional abnormalities, or discrepancy between electrographic findings and structural or functional imaging data).

The most promising alternative to the Wada test is functional magnetic resonance imaging (fMRI).[48] Functional MRI can display regions of increased blood flow (reflecting increased neuronal activity) in association with the performance of a task. These regions are presumed to be activated by the task in question. The judicial use of control tasks allows the identification of regions that are specifically activated by linguistic processing or memory encoding, rather than sensory perception or motor activity. Functional MRI has been demonstrated to lateralize language function in agreement with the Wada test in the vast majority of patients.[49-51] When the Wada and fMRI results diverged, the source of disagreement was usually one test indicating bilateral language distribution, while the other indicated unilateral dominance.[51] Improvements in the testing paradigm and control task, as well as use of a combination of tasks promises to further enhance fMRI.[48,51] Among the advantages of fMRI over the Wada test are its safety, its ability to localize areas with high resolution, and the potential for repeating studies with no added risk. However, much less has been carried out with fMRI memory testing. There have been studies indicating that the fMRI activation during memory items may have a lateralizing value in temporal lobe epilepsy. Functional MRI still has to be refined for testing of memory reserves.[20,52-54] Less has been carried out with respect to identification of memory reserves in the contralateral hippocampus and identification of patients at risk of postoperative amnesia.[48,55]

The Wada test is not always necessary prior to epilepsy surgery, but provides complementary and supportive data that improves the confidence of the presurgical evaluation. However, the Wada test has limitations, risks, and discomforts, and it is likely that in the future, fMRI may become the method of choice for routine preoperative assessment of language and memory, while the Wada test will remain an option for difficult patients.[56]

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